The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 5-6, 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takayama et al. (US 2003/0165812) in view of Gordon (US 5,627,066).

1. Re Claim 1, Takayama et al. discloses an integrated microfluidic sperm isolation device 1 comprising

- at least two gravity pump liquid reservoirs (paragraph [0049], line 2), one of said reservoir being a sperm receiving reservoir (motile particle supply reservoir 2; Figure 1; paragraph [0020], line 3), one of said reservoirs being a sort media liquid reservoir (media reservoir 3; Figure 1; paragraph [0020], line 4);
- at least one sort channel, said sort channel 6 (Figure 1; paragraph [0020], line 8) having a sort side (corresponding to side of media stream inlet channel 8) and a reject side (corresponding to side of sort stream inlet channel 7) (Figure 1; paragraph [0020], line 10), and an upstream portion in fluid communication with said sperm receiving reservoir on said reject side of said sort channel, and in fluid communication with at least one sort media reservoir on said sort side of said sort channel (Figure 1; paragraph [0022], lines 9-14);

- a rejected sperm receiving reservoir (motile particle-depleted sort stream reservoir 4; Figure 1; paragraph [0020], lines 5-6) in fluid communication with said downstream portion of said sort channel on said reject side of said sort channel (Figure 1);
- a sorted sperm reservoir (motile particle-enriched stream outlet 5; Figure 1; paragraph [0020], lines 6-7) in fluid communication with said downstream portion of said sort channel on said sort side of said sort channel (Figure 1), and
- sperm-containing liquid in said sperm receiving reservoir and a sort media liquid in a second reservoir exhibit gravity induced co-laminar flow of both liquids through said sort channel in parallel but separate streams having an interface therebetween, wherein motile sperm cross said interface and are ultimately transported in said sort media liquid to said oocyte insemination chamber from said sort channel or from said sorted sperm reservoir (Figure 2a-c; paragraph [0022]. lines 9-17).

Takayama et al. does not disclose an oocyte insemination chamber sized to contain one or more oocytes and into which sorted sperm flows, said chamber configured to contain at least one barrier which prevents egress of oocyte(s) located in said chamber but which is configured to allow fluid flow into or through said chamber, wherein said oocyte insemination chamber and said sorted sperm reservoir may together be a single chamber. Gordon teaches sperm samples 34 swimming to oocytes 33 in oocyte chambers 4, fertilizing the oocytes present (effectively causing the oocyte

insemination chamber and sorted sperm reservoir becoming a single chamber) (Col 4, lines 31-33) and the oocyte chambers 4 have such shapes such as a vortex shape (Col 4, lines 43-45 and 53-54) that keeps the oocytes within a particular location while allowing the motile sperms to swim to the oocytes.

Therefore, it would have been obvious to one skilled in the art at the time the invention was made to modify Takayama et al., to include a chamber that contains oocytes at the end of the sorted sperm stream with barriers, as taught by Gordon, in order to fertilize an oocyte in vitro in one set-up/environment.

2. Re Claim 2, Takayama et al. also discloses the device 1 being constructed of silicone elastomer (paragraph [0045], lines 3-5).

3. Re Claim 5, Gordon also teaches a barrier comprises a three dimensional barrier grate having forming plurality of barrier flow channels, said barrier flow channels smaller than an oocyte diameter by an amount such that said oocyte is blocked from passing through said barrier flow channels, but larger than the size of sperm such that sperm may travel through said barrier (Col 4, lines 43-45 and 53-54).

4. Re Claim 6, Takayama et al./Gordon discloses a method for in vitro insemination of an oocyte with sorted, motile sperm with minimal manipulation of said oocyte, said method comprising:

- selecting a device of claim 1;
- introducing one or more oocytes into said oocyte insemination chamber (Gordon; Col 4, line 22);

- introducing a first sperm-containing liquid to be sorted into a second sperm-containing liquid containing sperm of higher average motility than sperm of said first sperm containing liquid (Takayama et al.; paragraph [0023], lines 6-8);
- introducing a sort media liquid into said sort media liquid reservoir (Takayama et al.; paragraph [0022], lines 5-6);
- flowing said first sperm-containing liquid and said sort media liquid co-laminarly through said sort channel (Takayama et al.; paragraph [0022], lines 9-12);
- removing from said sort channel said second sperm-containing liquid (Takayama et al.; paragraph [0025], lines 1-4); and
- contacting said second sperm-containing liquid with said oocyte(s) (Gordon; Col 4, lines 31-33).

It would have been obvious at the time of the invention was made that when Takayama et al. was modified with Gordon, the resulting device of claim 1 would be able to perform the above mentioned steps due to the structure and function of the device.

5. Re Claim 11, Takayama et al. also discloses a growth media liquid being introduced into at least one of said gravity pump liquid reservoirs to provide a flow of growth media past said fertilized oocyte(s) (Paragraph [0027], lines 1-7).

6. Re Claim 12, Takayama et al./Gordon discloses a method for improving the rate of fertilization of oocytes when employing low sperm concentration, comprising

introducing one or more oocytes into a microfluidic channel, said channel having disposed therein a barrier having openings therein through which liquid and sperm may flow, but which are too small to allow an oocyte to enter (Gordon; Col 4, lines 43-45 and 53-54); introducing liquid and causing said oocyte(s) to travel through said channel to said barrier; introducing a sperm-containing liquid of low sperm concentration into said channel and flowing said sperm-containing liquid past said oocyte(s) (Gordon; Col 4, lines 31-33), wherein the rate of fertilization at the sperm concentration used is higher than the rate achieved in center-well fertilization.

7. Re Claim 13, Takayama et al./Gordon discloses the claimed invention except for the sperm concentration is less than $0.5x10^6$ sperm/mL. Gordon teaches that low sperm counts are $20x10^6$ sperm/mL or substantially less (Col 9, lines 65-66). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Takayama et al./Gordon to utilize sperm counts, even those that are low, since it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. In re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

8. Claims 3-4 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takayama et al./Gordon in view of Beebe et al. (US 6,193,647).

9. Re Claim 3 and 4, Takayama et al./Gordon discloses all of the claimed elements, except for having an oocyte duct communicating with said oocyte insemination chamber/sorted sperm reservoir. Beebe et al. teaches a well 42 which is in fluid

communication with a microfluidic channel 14 is used for the insertion or removal of embryo 16 (embryo is a fertilized oocyte, thus an oocyte can be used in place of an embryo) (Col 5, lines 62-67). Therefore, it would have been obvious to one skilled in the art at the time the invention was made to modify Takayama et al./Gordon to include an oocyte duct or well, as taught by Beebe et al., for the purposes of facilitating and the introduction and removal of oocytes/embryos from any chamber or location.

10. Re Claim 7, Takayama et al./Gordon discloses all of the claimed elements, except for the method of claim 6 comprising introducing said oocyte(s) into said oocyte insemination chamber through said oocyte duct, and removing one or more sperm-contacted oocytes from said oocyte insemination chamber through said oocyte duct. Beebe et al. teaches a well 42 in fluid communication with a microfluidic channel 14, into which embryos 16 are inserted or removed (embryo is a fertilized oocyte, thus an oocyte can be used in place of an embryo) (Col 5, lines 62-67). The oocyte duct/well 42 can easily be attached to an oocyte insemination chamber and the oocytes can be introduced at the beginning of the process and removed once fertilized at the end of the process. Therefore, it would have been obvious to one skilled in the art at the time the invention was made to modify Takayama et al./Gordon to include an oocyte duct or well connected to an oocyte insemination chamber, as taught by Beebe et al., for the purposes of guiding the instrument inserting and removing oocytes/embryos.

11. Re Claim 8, Takayama et al./Gordon also discloses that sperm-contacted oocyte is a fertilized oocyte (Gordon,; Col 4, lines 31-33)..

12. Re Claim 9, Takayama et al./Gordon discloses all of the claimed elements, except for introducing and removing of said oocyte(s) from said oocyte insemination chamber are performed with a pipette. Beebe et al. teaches inserting and removing oocytes/embryos 16 via pipette 44 (Col 6, lines 5-7). Therefore, it would have been obvious to one skilled in the art at the time the invention was made to modify Takayama et al./Gordon to include the usage of a pipette, as taught by Beebe et al., in order to use an easy and convenient way for moving oocytes from location to location.

13. Re Claim 10, Takayama et al./Gordon discloses all of the claimed elements, except for the oocyte insemination chamber being configured such that a plurality of oocytes occupying said chamber are forced to assume serial positions with respect to the direction of fluid flow. Beebe et al. teaches embryo 16 being placed in a microfluidic channel 14 that has biological medium (Col 6, lines 2-4) with flow and embryos rolling and sliding along the channels in the direction of the flow (Col 8, lines 57-61). Since oocytes would be placed one at a time, the oocytes would move serially along the flow of fluid. Therefore, it would have been obvious to one skilled in the art at the time the invention was made to modify Takayama et al./Gordon to include a configuration within the oocyte insemination chamber, as taught by Beebe et al., for the purposes of having an organized environment in which the oocytes are fertilized.

14. The declaration under 37 CFR 1.132 filed 7/06/09 is insufficient to overcome the rejection of claims 1-13 based upon Takayama et al (2003/0165812) as set forth in the last Office action because: the declaration was submitted to provide a

showing that the Takayama et al reference (2003/0165812) is not proper prior art and therefore the rejection can not be maintained. However the declaration, specifically "part 3", is incorrect, part 3 states that Shuichi Takayama is a co-inventor with 3 other inventors (Gary Smith, Timothy Schuster and Brenda "Shen" (which should be Cho)) on U.S. Patent Application No. 10/559,742 filed June 7, 2004. However 10/559,742 has listed invertors Takayama, Smith and Suh not the above listed inventors and was filed May 24, 2006 not June 7, 2004. Also should applicant have intended to list the Takayama et al reference that was actually used in the prior art rejection (10/375,373) or Publication Number 2003/0165812, while the inventors listed would be proper (except for the misspelling of Brenda S. Cho) this application also was not filed on June 7, 2004 as is stated in the declaration. Since the declaration is considered to be insufficient the rejection is maintained.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John P. Lacyk whose telephone number is (571)272-4728. The examiner can normally be reached on 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Chuck Marmor, II can be reached on 571-272-4730. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

J.P. Lacyk

/John P Lacyk/
Primary Examiner, Art Unit 3735